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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,628	09/05/2006	Hirohiko Hohjoh	U 016154-7	2748
140	7590	12/28/2010	EXAMINER	
LADAS & PARRY LLP 26 WEST 61ST STREET NEW YORK, NY 10023			CHONG, KIMBERLY	
			ART UNIT	PAPER NUMBER
			1635	
			NOTIFICATION DATE	DELIVERY MODE
			12/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No. 10/568,628	Applicant(s) HOHJOH, HIROHIKO	
	Examiner KIMBERLY CHONG	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,9-18 and 22-27 is/are pending in the application.
- 4a) Of the above claim(s) 24,25,27 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,9-18,22,23 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/02/2010, 08/31/09</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/02/2010 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 09/02/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 09/13/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed 09/02/2010, claims 1-5, 9-18 and 22-28 are pending, claims 24-25 and 27-28 are withdrawn and claims 1-5, 9-18, 22-23 and 26 are currently under examination.

Information Disclosure Statement

The submission of the Information Disclosure Statements on 09/02/2010 and 08/31/2009 are in compliance with 37 CFR 1.97. The information disclosure statement has been considered by the examiner and signed copies have been placed in the file.

New Claim Objections and Rejections

Claim Objections

Claim 1 is objected to because of the following informalities: the limitation “which is improved based on a conventional siRNA consisting of complement complementary sense and antisense strands” would be better phrased by stating the dsRNA is improved *as compared to* a conventional siRNA. This phrasing is a suggestion and as a reminder to Applicant, any claim amendment must have support in the instant specification.

There appears to be the word "and" missing between the word "part" and "only" in the 5th line of the claim.

The word “nucleotide” in the 5th line of the claim is a misspelling of the word nucleotide.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 9-18, 22-23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection which is necessitated by new claim amendments.

Claim 1 recites “only one or more consecutive nucleotides at the ends of the double-stranded part “. Applicant points to support for these claim amendments in paragraph 022-0030. The instant specification , particularly in these paragraphs, do not provide support for the mismatch nucleotides to be consecutive and do not provide support for the mismatch nucleotides to be on both ends of the dsRNA.

Furthermore the amendment filed 09/02/2010 represents a departure from the claims as originally filed. If Applicant believes that such support is present in the specification and claimed priority documents, Applicant should point, with particularity, to where such support is to be found.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and all dependent claims 2-5, 9-18, 22-23 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in the 5th line that only one nucleotide "at around the center of the double-stranded part". This phrase is ambiguous because either the nucleotide is at the center or it is around the center of the double-stranded part. For purposes of applying prior art, the mismatched nucleotide is interpreted to mean it is around the center of the double-stranded part of the strand.

Further the limitation "at around the center of the double-stranded part or both in said RNA" is unclear. The reference to "both" has no meaning in the sentence and is vague and ambiguous.

Response to Arguments

Claim Rejections - 35 USC § 102 - maintained

The rejection of claims 1-5, 9-18, 22-23 and 26 under 35 U.S.C. 102(e) as being anticipated by Zamore et al. (US 2005/0186586 cited on PTO Form 892 mailed 01/24/2008) as evidenced by Aravin et al. (Developmental Cell, 2003 cited on PTO Form 892 mailed 01/24/2008) and Elbashir et al. (Nature 2001 cited on PTO Form 892 mailed 01/24/2008) is maintained for the reasons of record.

Applicant's arguments filed 09/02/2010 have been fully considered but they are not persuasive. Applicant argues the invention as amended is clearly different that the structures cited in Zamore et al. as the claimed invention is limited to one or more consecutive residues at the center of the double-stranded part and have been amended to exclude mismatches at any other position.

The claims are interpreted as follows: the dsRNA is interpreted such that the one or more consecutive nucleotides "at the ends of the double-stranded part" is not required to be at both ends and can still be at either the 3' or 5' end. The nucleotide at around the center of the double stranded part is interpreted as explained above such that nucleotide is around the center. The limitation wherein the claimed dsRNA is improved based on a conventional siRNA would be an inherent feature if the claimed structure is taught in the art.

Regarding the limitation wherein the dsRNA has only one or more consecutive nucleotides that are mismatched, Zamore et al. teach a dsRNA comprising a sense and antisense strand wherein up to 4 nucleotides on the sense strand are not complementary to the antisense strand (see Figure 6A, siRNA molecules miR-13b-2 and miR-124a for example). This meets the limitations of "only one or more consecutive nucleotides".

Zamore et al. teach a dsRNA having a mismatch at positions 11 (see Figure 6A miR-13b-2) or a dsRNA having only one nucleotide and one additional nucleotide located at 11-13 (see Figure 6A, specifically mir-6-3). Thus, this meets the limitation of "only one...nucleotide" and "one additional nucleotide located at 11-13".

Therefore Zamore et al. anticipates the instant claims and the rejection is maintained.

Claim Rejections - 35 USC § 103 - maintained

The rejection of claims 1-5, 9-18, 22-23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jayasena et al. (US 20040248299), Khvorova et al. (US 2007/0031844), Elbashir et al. (EMBO Journal 2001, Vol. 20, No. 23: 6877-6888) and Holen et al. (Nucleic Acids Research 2002, Vol. 30, No. 8: 1757-1766) is maintained for the reasons of record.

Applicant's arguments filed 09/02/2010 have been fully considered but they are not persuasive. Applicant continues to argue that it was well known in the art that single stranded RNA is more susceptible to degradation by RNase than double stranded RNA and if the structure had mismatches on the end the siRNA would be expected to be easily degraded and those skilled in the art would never try to incorporate mismatches into siRNA molecules. Applicant argues the mismatches disclosed by Elbashir et al. and Holen et al. are between the antisense strand of siRNA and the target mRNA and not between the antisense strand and the sense strand.

Applicant's arguments are not convincing. First of all, the mismatches at the ends of the dsRNA are designed such that the duplex region is associated but that the association between the mismatched bases is weaker to allow for unwinding and preferential loading of the proper guide strand into RISC therefore the ends are not single stranded. It was clearly recognized by Jayasena et al. and Khvorova et al. that mismatches at the ends of the duplex allowed for the antisense guide strand to more efficiently load into RISC and therefore the skilled artisan would incorporate mismatches into siRNA molecules to increase the efficiency of the guide strand entering RISC.

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thereby increasing the efficiency of RNAi. Furthermore it was well known in the art, and taught by Jayasena et al., Khvorova et al. and Elbashir et al., that incorporation of chemical modifications of dsRNA molecules protected the molecule against degradation by nucleases and the skilled artisan would be capable of designing stable dsRNA while improving the efficiency of RNAi by incorporation of mismatches at the ends of the duplex. Furthermore, one of ordinary skill in the art would have recognized from Holen et al. the desirability to investigate the tolerance of the RNAi system for mismatches in the siRNA relative to the mRNA target.

In regard to Applicant's argument that the mismatches taught by Elbashir et al. and Holen et al. are between the antisense strand and the target mRNA, this argument is not convincing. The sense strand of a dsRNA used to inhibit the expression of a mRNA is designed to contain the exact sequence of the target mRNA (see the cited references), therefore the antisense strand with a mismatch to the target would in fact also have a mismatch to the sense strand. Figure 6 of Holen et al. clearly exemplify a dsRNA with one or two mismatches relative to the sense strand which would also be mismatches relative to the target sequence. Moreover, the teachings of Elbashir and Holen et al. are taken as a whole with the other cited references who do in fact clearly teach a reason to incorporate mismatched nucleotides into a dsRNA.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Acting SPE for 1635 Heather Calamita at 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Primary Examiner
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